



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

MC

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/816,242 | 04/01/2004 | James Freddo | PC25581A | 9207 |

28940 7590 10/18/2007
PFIZER INC
10555 SCIENCE CENTER DRIVE
SAN DIEGO, CA 92121

| |
|----------|
| EXAMINER |
|----------|

GEMBEH, SHIRLEY V

| | |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1614

| | |
|-----------|---------------|
| MAIL DATE | DELIVERY MODE |
|-----------|---------------|

10/18/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/816,242 | Applicant(s) FREDDO ET AL. | |
| | Examiner Shirley V. Gembel | Art Unit 1614 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 January 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8-16, 32-41, 46 and 49-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8-16, 32-41, 46 and 49-51 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The response filed **8/7/07** presents remarks and arguments to the office action mailed **4/11/07**. Applicants' request for reconsideration of the rejection of claims in the last office action has been considered.

Applicants' arguments, filed, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of Claims

Claims 8-16, 32-41, 46 and 49-51 are pending in this office action.

Claims 49-51 are newly added.

Claim Objections

Claim 32 is objected to for the following informalities: the terms "VEGF-, PDGF-, c-Kit", should be spelled out when first used. Appropriate correction is required.

Maintained Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 32-41 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating animals, beagle dogs and mice for the treatment of breast cancer, lung cancer cells and or human umbilical vein endothelial cells, does not reasonably provide enablement for treating a wide variation of cancer with the claimed compound in humans. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The invention is drawn to methods of treating abnormal cell growth or cancer in a patient, comprising administering the instant compound of formula I to a patient in need thereof. However, the claims recite any or a large variety of abnormal cell growth or cancers.

The amendment to claim 32 to recite VEGF-, PDGF or c-kit related cancers does not obviate the above rejection. As has been shown by Voskoglou-Nomikos et al. Clinical Cancer Research, Vol. 9, 4227-4239, which is presented for evidentiary purpose only, teach a human xenograft model demonstrating a good tumor –specific predictive value for non-small cell lung cancer and ovarian cancer. See abstract and page 4236 underlining. Panels of xenograft were used but failed to adequately predict clinical performance both in disease and in a compound-oriented approach.

Applicant has not shown how the compound of formula I is capable of treating a wide variety of cancers. Applicant asserts that the use of anti-angiogenic agents to treat VEGF-, PDGF or c-kit related cancers, that rely on angiogenesis is a common

Art Unit: 1614

strategy in the pharmaceutical arts (see Senger, Am. J. Pathol. 149:1-7 (1996) - Exhibit 1). However, it is also true that no one drug has been used successfully in the treatment of cancers of diverse etiology. The terms VEGF-, PDGF or c-kit related cancers are known in the art; however, tumor proliferation is complex and unpredictable. The cellular and molecular mechanisms that regulate vessel development in tumors are often unknown. Clearly, this one drug does not have the capability of exhibiting all of the asserted functions in every cancer.

Applicants' argument is unpersuasive, and rejection is maintained.

It is suggested that the claims are limited to those specific cancers having clear support in the specification.

Claim Rejections - 35 USC § 102

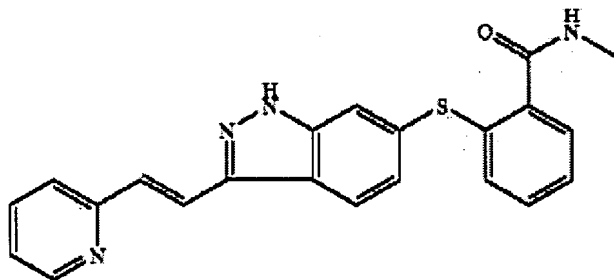
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Kania et al. WO 2001/02369 (now a US Patent 6,531,491).

Kania et al. teach administering a composition comprising a compound of formula 1, as shown below, to a mammal (see col. 16, lines 25+).



See col. 11, lines 35+ where a pharmaceutically acceptable salt or solvate (see col. 13, lines 19-30) is disclosed. The reference also teaches administering the compound orally (see col. 21, lines 56), as in claim 15, in a tablet or capsule, as in claims 7 and 16. The dosage preferred in the reference is 0.001-50 mg, thus anticipating claims 8-14 (see col. 21, lines 30+).

Applicant again argues that the cited reference does not teach the claimed dosage forms, as recited in the claims, and that the cited reference discloses a generic range of 0.001-50 mg/kg.

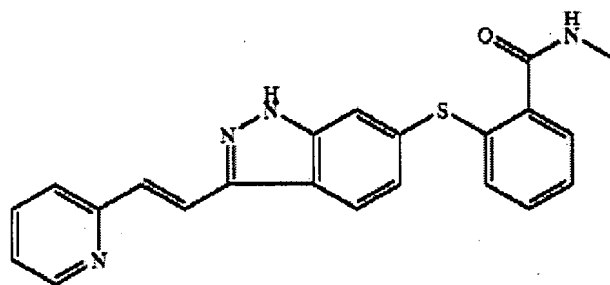
This argument is traversed, and as stated in the last office action, the mere fact that the cited art discloses a range of dosages clearly indicates that any range within that taught by Kania is capable of been used.

For example, for the limitation of instant claim 8, from 0.5-30 mg, if a patient weighs 70 kg, and 0.4 mg per kg is administered, 28 mg is the dose, which is well within the claim limitation. Subsequently, the ranges can be regulated to fall within the claim limitation of 8-14. The cited ranges are anticipated in the references.

Claims 32-41 and 46 rejected under 35 U.S.C. 102(b) as being anticipated by Kania et al. WO 2001/02369 now a US Patent 6,531,491.

Art Unit: 1614

Kania et al. teach methods of treating cancer ,and other disease states associated with unwanted angiogenesis and/or cellular proliferation (see abstract), via administering a compound of formula 1, as shown below, to a mammal (see col. 16,



lines 25+)

See col. 11 lines 35+ where a pharmaceutically acceptable salt or solvate (see col. 13, lines 19-30) is disclosed. The reference also teaches administering the compound orally (see col. 21, lines 56) as in claims 22 and 39. The dosage preferred in the reference is 0.001-50 mg, thus anticipating claims 32, in part, and 33-38 (see col. 21, lines 30+).

Applicant argues that Kania refers to methods of using the compounds disclosed therein for treating various types of cancer. As discussed above, however, this disclosure is provided in a generic sense with reference to all of the compounds in Kania, and is not specifically directed to the compound of formula I. Furthermore, Kania does not disclose the use of the specific compound of formula I for treating cancer using the specific dosage amounts as recited in the present claims.

In response, this is found unpersuasive because the reference teaches the indazole compounds and pharmaceutical compositions for inhibiting protein kinase, and methods for their use. The compounds of formula IV in Kania's reference are included in instant formula I (see col. 8, lines 35-65). The dosage range for compound

Art Unit: 1614

of formula I is taught in column 21, lines 30+. Further, the reference teaches the indazole compounds are designed to treat angiogenesis by inhibiting kinase activity of VEGF. See col. 20, lines 12-15.

Claim Rejections - 35 USC § 103

Claims 32-41 and 46 were rejected under 35 U.S.C. 103(a) in the last Office Action as being unpatentable over Kania et al. WO 2001/02369, now a US Patent 6,531,491.

The rejection is withdrawn based on Applicants' showing of unexpected results with respect to Exhibit 2.

Double Patenting

Claims 8-16, 32-41, 46 and 49-51 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim **1 - 11** of U.S. Patent **7141581**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

Both applications recite using the same compositions and/or derivatives thereof. See instant application claims 8-16, 32-41, 46 and 49-51 and copending application claims 1 – 11. The compositions recited in the claims are obvious of each other for the treatment of various types of cancers.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

Applicant argues that the patented claims are to a method of treatment with various compounds and without any specific dosing range.

This is found unpersuasive. The claims recite a range, and one of ordinary skill in the art would have been motivated to optimize the dosage and administer an optimal dosage to the patient in need thereof. The specification of the patent, when used as a

Art Unit: 1614

dictionary, (see col. 25, lines 24-30) teaches an amount of a given agent that corresponds the dosage range claimed in the instant application. The amount will vary depending upon factors such as the particular compound, disease condition and its severity, the patient's age and weight of the mammal in need of treatment, but can nevertheless be routinely determined by one skilled in the art.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

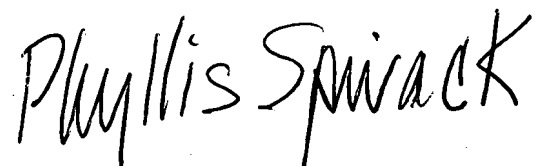
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembah whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1614

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


SVG
10/04/07



**PHYLLIS SPIVACK
PRIMARY EXAMINER**